

Applicants: Randy S. Bethel et al.
Application No.: 10/700,936

REMARKS

The Claim Amendments

Applicants have amended claim 26 to recite a method of inhibiting JAK3 in a biological sample. Applicants have amended claim 28 to incorporate the limitations of canceled claim 27 and to more clearly define their invention. Applicants have also amended claim 29 to more clearly define their invention. Support for these amendments may be found throughout the specification and in the originally-filed claims. None of these amendments adds new subject matter. Their entry is requested.

These claim amendments are made expressly without waiver of applicants' rights to continue to prosecute and to obtain claims to the canceled subject matter either in this application or in other applications claiming benefit herefrom.

The Response

Applicants thank Examiner Habte for telephoning to indicate that claims 1-24 were allowable and that claims 26-29 would be rejoined with the elected invention. In the telephone call, Examiner Habte indicated that while the specification enabled methods of treating allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease and rheumatoid arthritis, it did not enable, *inter alia*, leukemia. Applicants traverse.

The specification fully enables one skilled in the art to practice the method of treating leukemia by administering a compound of the invention or a pharmaceutical composition thereof. The method is supported by the specification as filed, which demonstrates that the claimed compounds have JAK inhibitory activity, and provides adequate guidance for administering compounds of the invention to a patient in need therenf. See, e.g., Example 16 on page 54-55 and pages 40-44 of the specification.

Further, various references support applicants' assertion that the compounds of the present invention may be used to treat a number of different leukemias. For instance, Sudbeck et al. (Clin. Cancer Res. 5: 1569-82, 1999) teaches that targeting JAK family

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kinases with specific inhibitors can inhibit proliferation of JAK3-expressing leukemic cell lines, including cell lines derived from pre-B cell acute lymphocytic leukemia (ALL), B cell ALL, T-cell ALL and acute myelogenous leukemia (AML). See, e.g., paragraph [0012] of the specification and pages 1578-81 of Sudhirk et al. Steelman et al. (Leukemia 18:189-218, 2004) discloses that JAK2 activation is involved in various leukemias, including chronic myelogenous leukemia (CML) and ALL. See, e.g., page 192 of Steelman et al. Further, Mahon (Oncogene 24: 7125-26, 2005) discloses that dysregulation of JAK2 is implicated in various leukemias, including myeloproliferative disorders such as CML, polycythemia vera, essential thrombocythemia and idiopathic myelofibrosis, as well as chronic myelomonocytic leukemia, atypical CML and acute leukemia. See, e.g., page 7125 of Mahon. Faderl et al. (Anticancer Research 25: 1841-50, 2005) also discloses that a JAK-STAT inhibitor has antileukemic and apoptotic activity in leukemic cell lines and in cells isolated from patients with acute myeloid leukemia (AML). See pages 1844-48 of Faderl et al. In summary, the references indicate that JAK is involved in a number of different types of leukemia and that JAK inhibitors may be used to inhibit proliferation of several leukemic cell types. Thus, in view of the teachings of the specification and the knowledge in the art at the time this application was filed, one skilled in the art would be able to practice the claimed methods without undue experimentation to treat a variety of leukemias.

The Examiner also indicated that the specification did not enable the method of administering an additional therapeutic agent as recited in claim 29. Applicants traverse.

The specification teaches how to administer the compounds of the invention in combination with other desired therapeutics or medical procedures and provides examples of various therapeutic agents that may be administered with compounds of the invention. See, e.g., pages 47-49. Further, administering a combination of drugs for particular diseases is well known to skilled practitioners and is commonly done. In addition, numerous chemotherapeutic or anti-proliferative agents, asthma treatments, anti-inflammatory agents and immunomodulatory or immunosuppressive agents are known for treating the claimed diseases. Examples of such agents are provided in the specification, but others are known to

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and commonly used by skilled artisans. Thus, given the guidance provided in the specification, combined with the high level of skill of the medical practitioners, one skilled in the art would be able to practice the claimed methods without undue experimentation.

Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying arguments, and allow the claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the Examiner contact the undersigned at his convenience.

Respectfully submitted,

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